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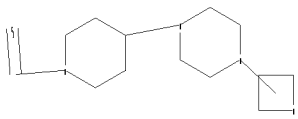

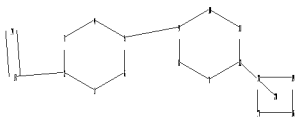

chain nodes :
13 14
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 16 17 18 19
chain bonds :
2-13 5-9 13-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 16-17 16-19 17-18 18-19
exact/norm bonds :
1-2 1-6 2-3 2-13 3-4 4-5 5-6 5-9 7-8 7-12 8-9 9-10 10-11 11-12 13-14 16-17 16-19 17-18 18-19
isolated ring systems :
containing 1 : 7 :

G1:O,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:CLASS 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 14:03:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1802 TO ITERATE

100.0% PROCESSED 1802 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 33494 TO 38586
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 14:03:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 34077 TO ITERATE

100.0% PROCESSED 34077 ITERATIONS 22 ANSWERS
SEARCH TIME: 00.00.01

L3 22 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'CAPLUS' ENTERED AT 14:04:02 ON 26 DEC 2007
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FILE COVERS 1907 - 26 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 25 Dec 2007 (20071225/ED)

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=> s l3
L4 1 L3

=> d l4 bib abs hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:550949 CAPLUS
DN 141:106497
TI Preparation of substituted 1-piperidin-4-yl-4-azetidin-3-yl-piperazine derivatives and their use as neurokinin antagonists
IN Janssens, Frans Eduard; Sommen, Francois Maria; De Boeck, Benoit Christian Albert Ghislain; Leenaerts, Joseph Elisabeth
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004056800	A1	20040708	WO 2003-EP51042	20031217
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2509406	A1	20040708	CA 2003-2509406	20031217
	AU 2003299249	A1	20040714	AU 2003-299249	20031217
	EP 1581517	A1	20051005	EP 2003-799583	20031217
	EP 1581517	B1	20070221		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006512349	T	20060413	JP 2004-561505	20031217
	AT 354572	T	20070315	AT 2003-799583	20031217
	ES 2282731	T3	20071016	ES 2003-3799583	20031217
	US 2006074069	A1	20060406	US 2005-540304	20050621
PRAI	WO 2002-EP14837	A	20021223		
	WO 2003-EP51042	W	20031217		

OS MARPAT 141:106497
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Q = O or NR3; X = covalent bond, -O-, -S-, or -NR3; R1 independently = Ar1, Ar1-alkyl, and di(Ar1)-alkyl; R2 = Ar2, Ar2-alkyl, di(Ar2)-alkyl Het1, Het1-alkyl; R3 independently = H or alkyl; Y = covalent bond, -CO-, -SO2-, >C:CHR or >C:NR, wherein R = H, CN or NO2; M independently = covalent bond, (un)substituted-alkyl, -(un)saturated carbocycle; L = H, alkyloxy, Ar3oxy, alkylamine, etc.; Ar1 = (un)substituted phenyl; Ar2 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, aminocarbonyl, and alkyloxy; Ar3 = (un)substituted naphthalenyl or Ph with substituent(s) selected from

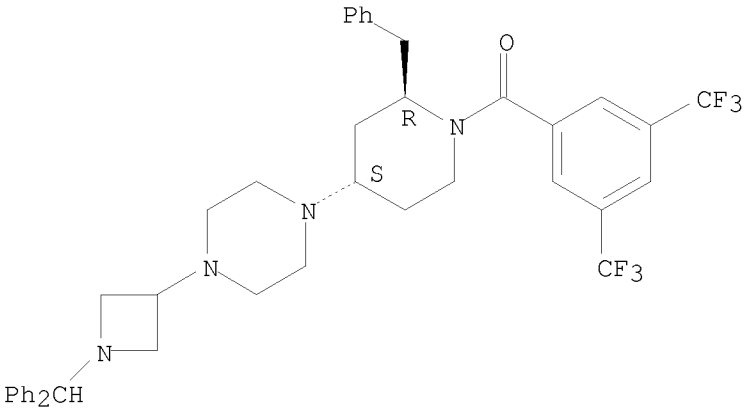
halo, alkyl, CN, amino, alkyloxy, OH, pyridinyl, etc.; Het1 = monocyclic heterocyclic radical selected from pyrrolyl, pyrazolyl, imidazolyl, furanyl, etc.; m = 1 or 2 provided that if m = 2, then n = 1; n = 0-2; p = 1-2; q = 0-1] and their pharmaceutically acceptable salts having neurokinin antagonistic activity, in particular NK1 antagonistic activity and NK1/NK3- antagonistic activity, their preparation, compns. comprising them and their use as a medicine, in particular for the treatment of schizophrenia, emesis, anxiety, depression, irritable bowel syndrome (IBS), circadian rhythm disturbances, pain, neurogenic inflammation, asthma, micturition disorders such as urinary incontinence and nociception are disclosed. Thus, e.g., II was prepared by reaction of (2R-trans)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-(1-piperazinyl)piperidine (preparation given) with 1-(diphenylmethyl)-3-azetidinyl methanesulfonate. For selected compds. of the invention, receptor binding pIC50 values for h-NK1 were in a range from 6.69-8.13. In view of their capability to antagonize the actions of tachykinins by blocking the neurokinin receptors, and in particular antagonizing the actions of substance P by blocking the NK receptors, the compds. according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of tachykinin mediated conditions, such as, for instance CNS disorders, in particular depression, anxiety disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, schizoaffective disorders, eating disorders, neurodegenerative diseases, addiction disorders, mood disorders, sexual dysfunction, pain and other CNS related conditions ; inflammation ; allergic disorders ; emesis ; gastrointestinal disorders, in particular irritable bowel syndrome (IBS); skin disorders ; vasospastic diseases ; fibrosing and collagen diseases ; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.

IT 718637-71-9P 718637-72-0P 718637-73-1P
718637-74-2P 718637-75-3P 718637-76-4P
718637-77-5P 718637-78-6P 718637-79-7P
718637-80-0P 718637-81-1P 718637-82-2P
718637-83-3P 718637-84-4P 718637-85-5P
718637-86-6P 718637-87-7P 718637-88-8P
718637-89-9P 718637-90-2P 718637-91-3P
718637-92-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stereoselective preparation of piperidinylazetidinylpiperazines with tachykinin antagonist activity)

RN 718637-71-9 CAPLUS

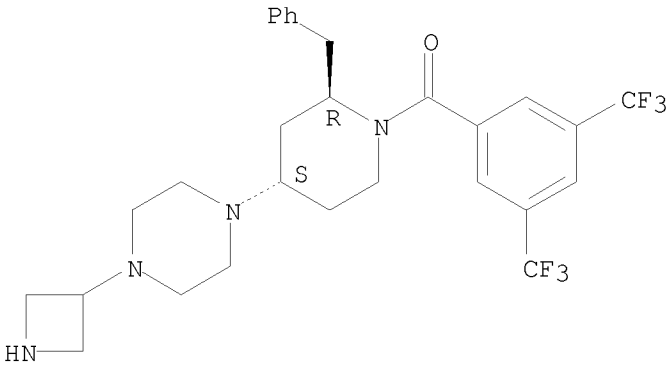
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(diphenylmethyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



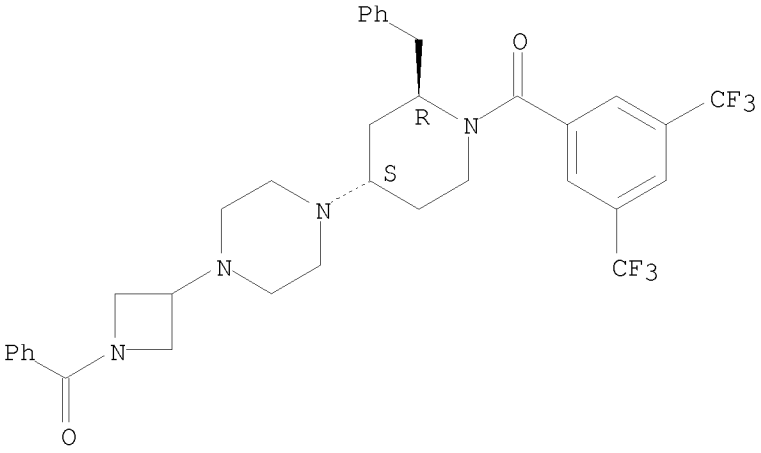
RN 718637-72-0 CAPLUS
CN Piperidine, 4-[4-(3-azetidinyl)-1-piperazinyl]-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



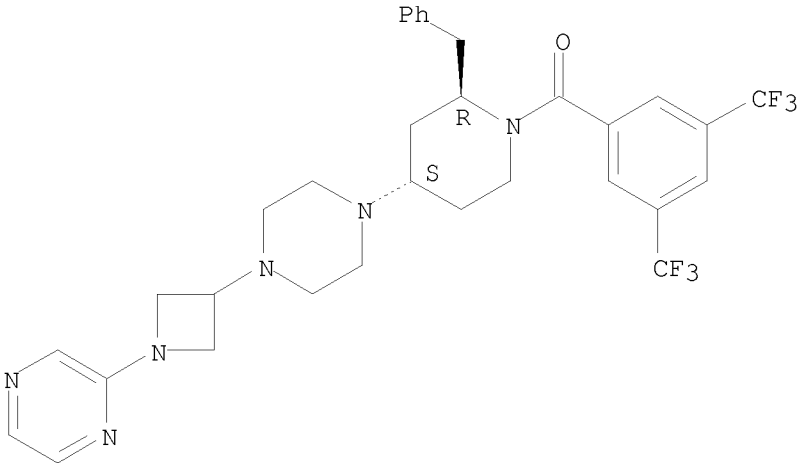
RN 718637-73-1 CAPLUS
CN Piperidine, 4-[4-(1-benzoyl-3-azetidinyl)-1-piperazinyl]-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



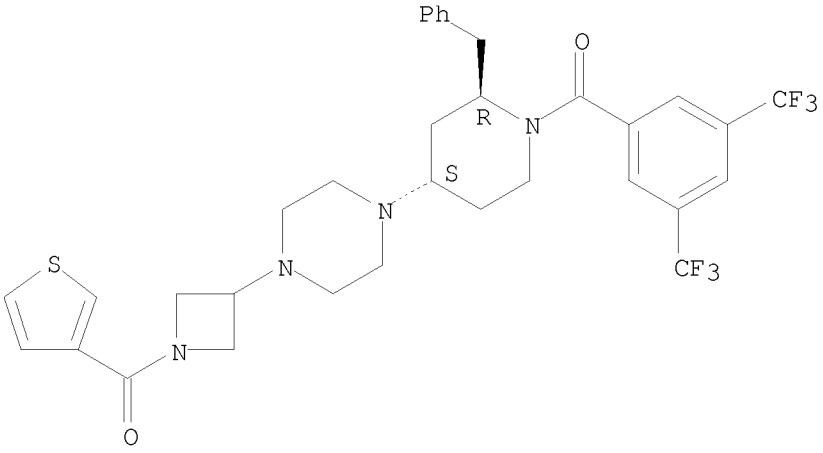
RN 718637-74-2 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-(1-pyrazinyl-3-azetidinyl)-1-piperazinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



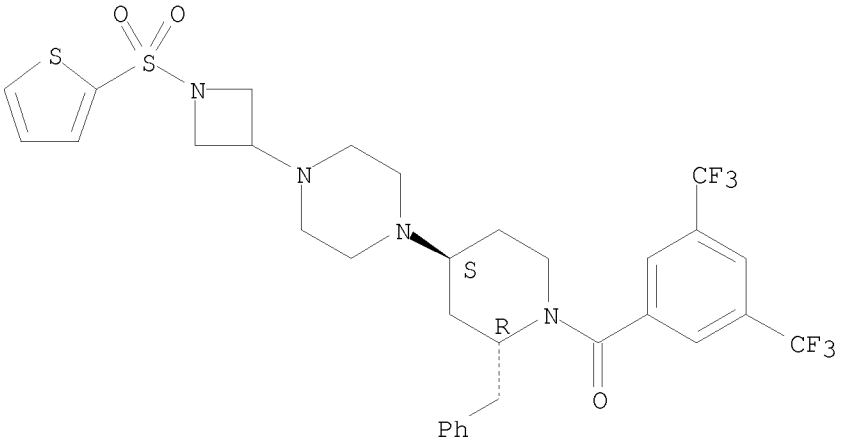
RN 718637-75-3 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[1-(3-thienylcarbonyl)-3-azetidinyl]-1-piperazinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



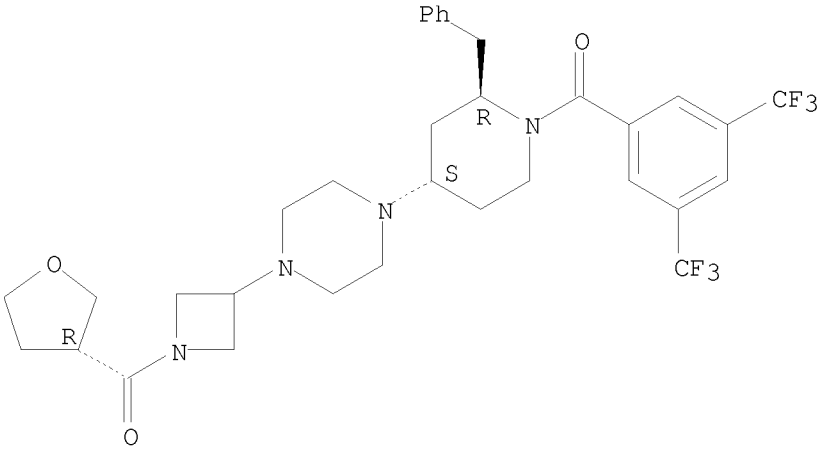
RN 718637-76-4 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[1-(2-thienylsulfonyl)-3-azetidinyl]-1-piperazinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



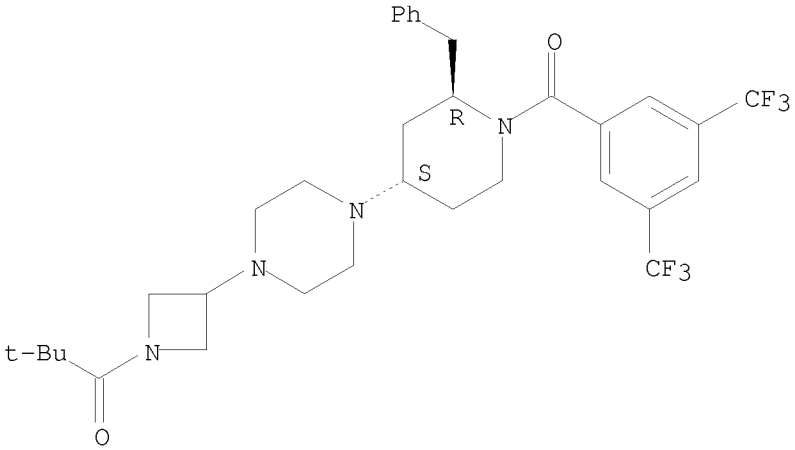
RN 718637-77-5 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[1-[[(3R)-tetrahydro-3-furanyl]carbonyl]-3-azetidinyl]-1-piperazinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



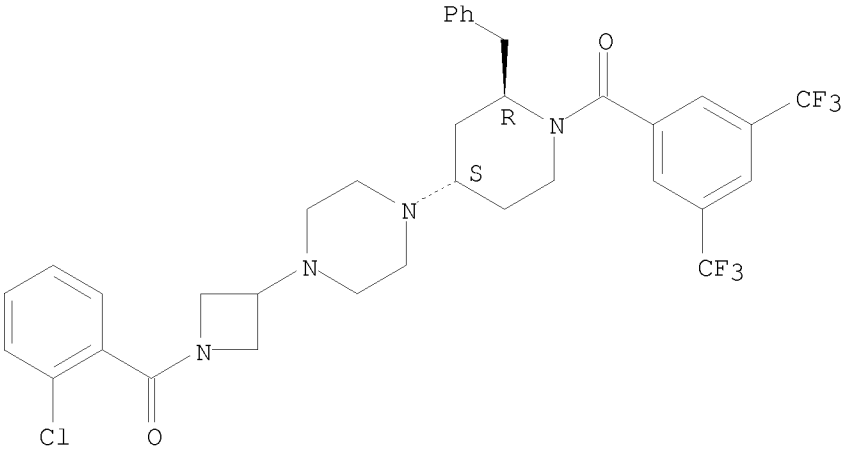
RN 718637-78-6 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(2,2-dimethyl-1-oxopropyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



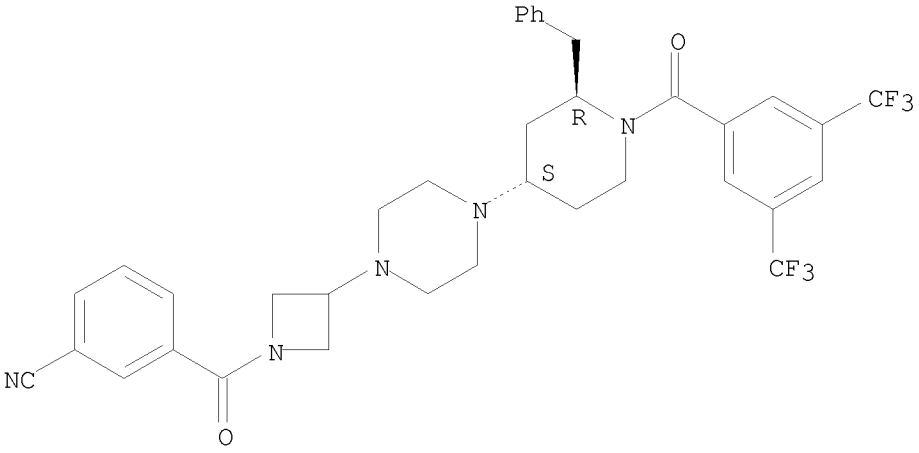
RN 718637-79-7 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(2-chlorobenzoyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



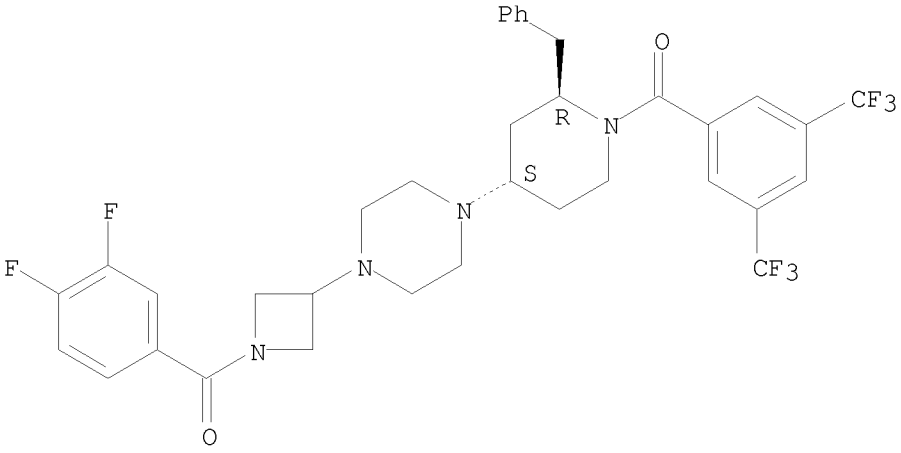
RN 718637-80-0 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(3-cyanobenzoyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



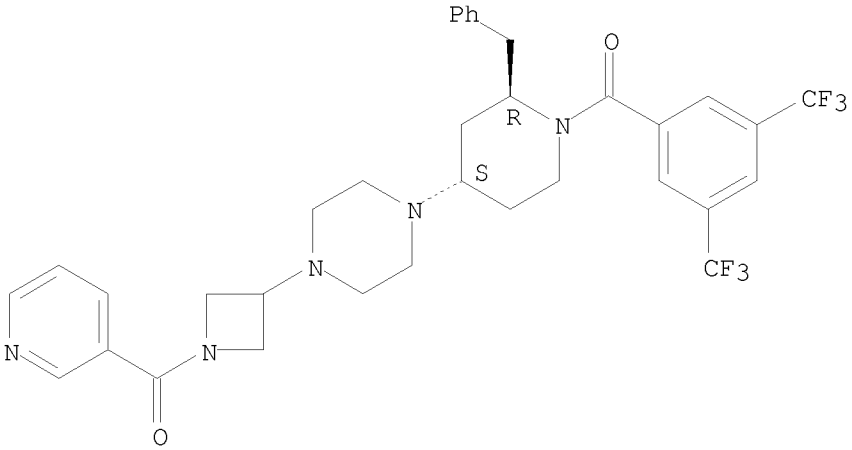
RN 718637-81-1 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(3,4-difluorobenzoyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



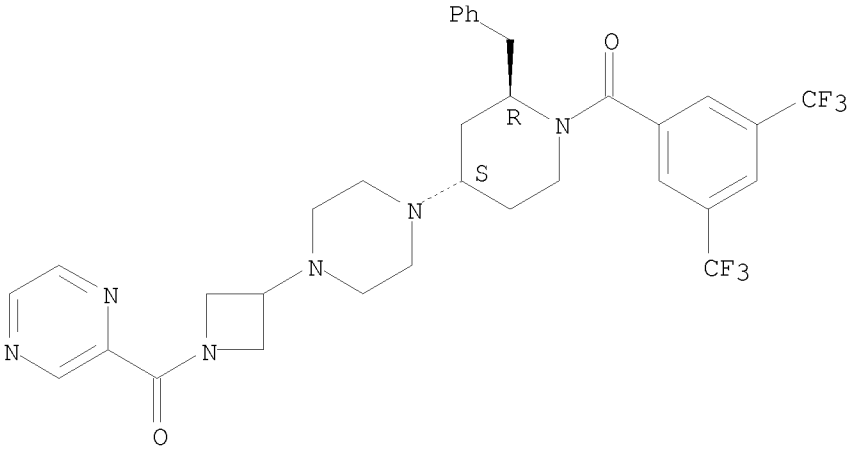
RN 718637-82-2 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[1-(3-pyridinylcarbonyl)-3-azetidinyl]-1-piperazinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



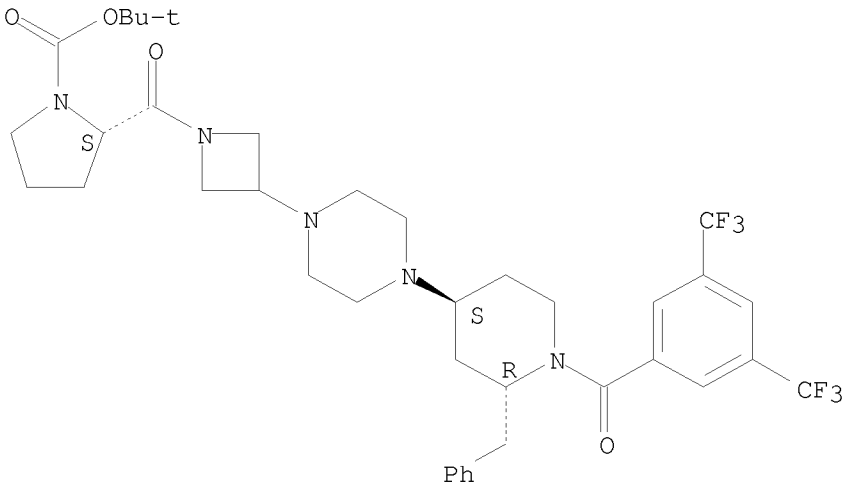
RN 718637-83-3 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[1-(pyrazinylcarbonyl)-3-azetidinyl]-1-piperazinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



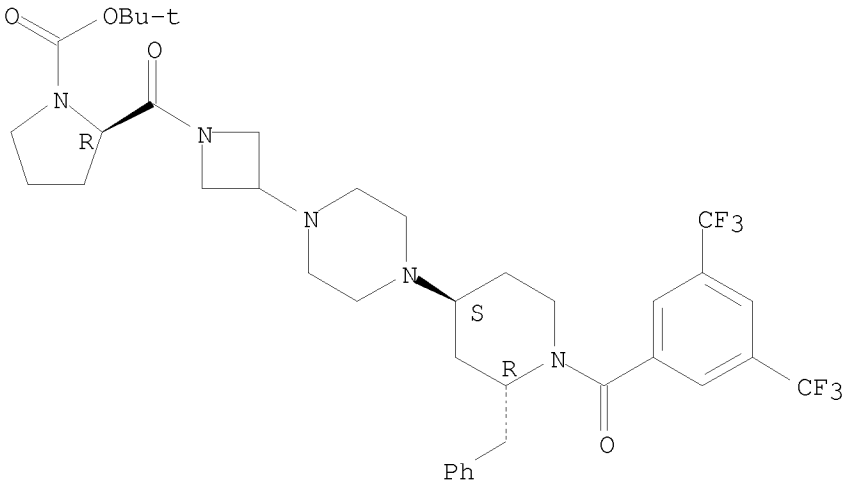
RN 718637-84-4 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[3-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]-1-azetidinyl]carbonyl]-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



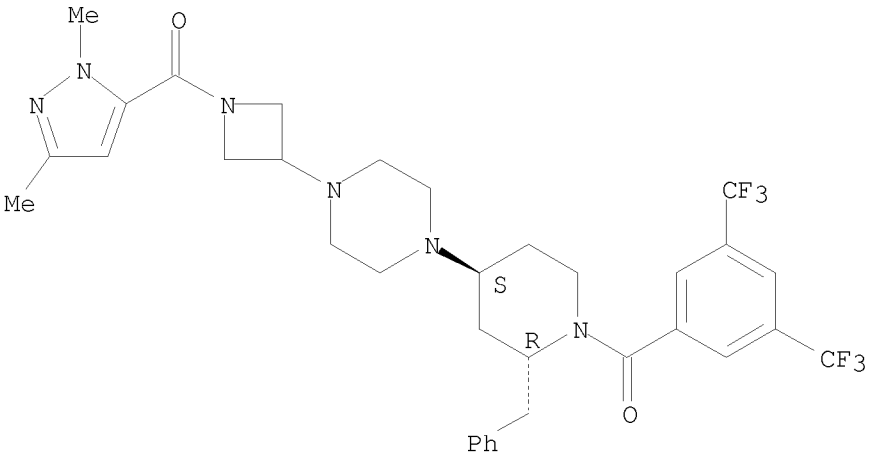
RN 718637-85-5 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[3-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]-1-azetidinyl]carbonyl]-, 1,1-dimethylethyl ester, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



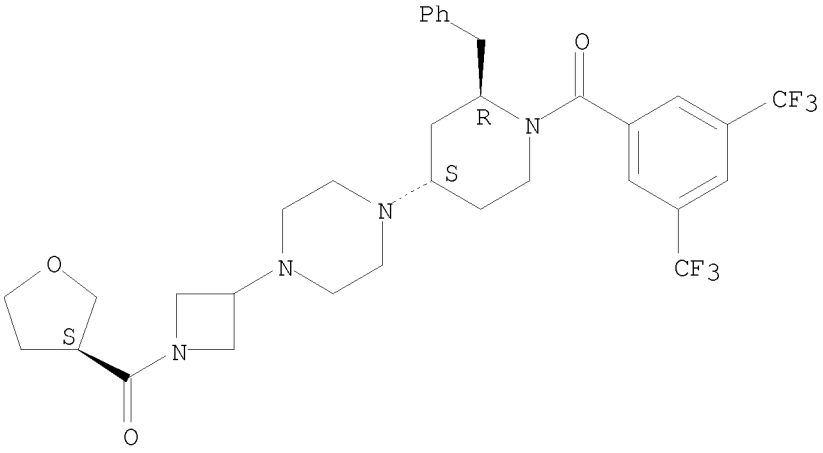
RN 718637-86-6 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-[(1,3-dimethyl-1H-pyrazol-5-yl)carbonyl]-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



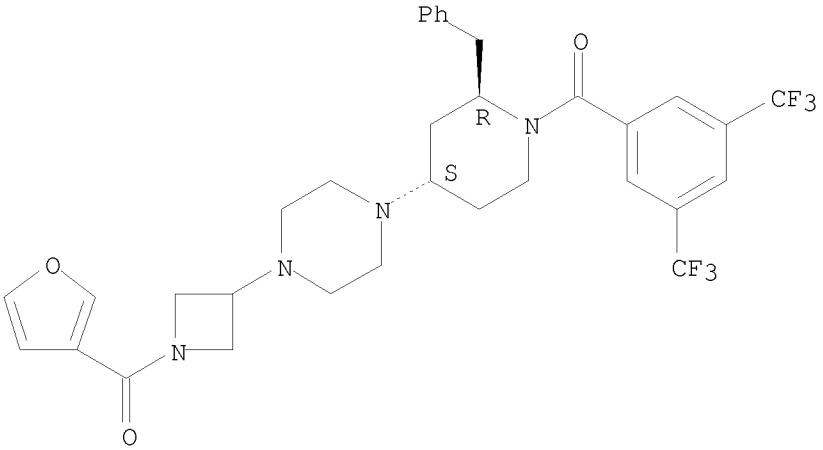
RN 718637-87-7 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[1-[[(3S)-tetrahydro-3-furanyl]carbonyl]-3-azetidinyl]-1-piperazinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



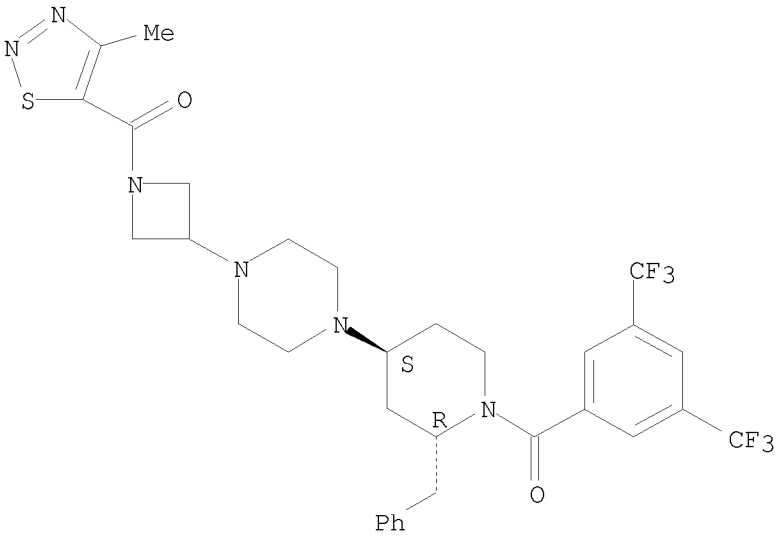
RN 718637-88-8 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(3-furanylcarbonyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



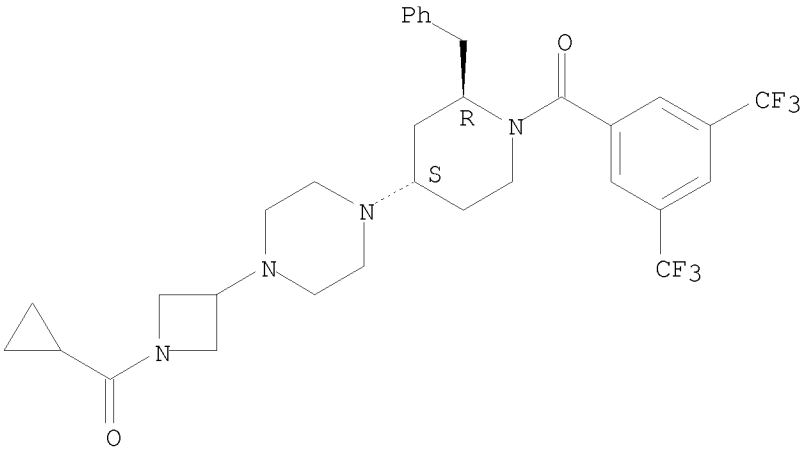
RN 718637-89-9 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-[(4-methyl-1,2,3-thiadiazol-5-yl)carbonyl]-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



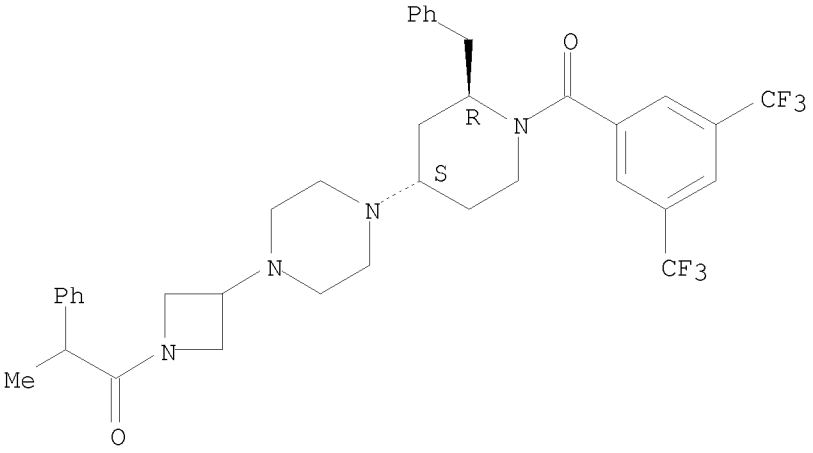
RN 718637-90-2 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(cyclopropylcarbonyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



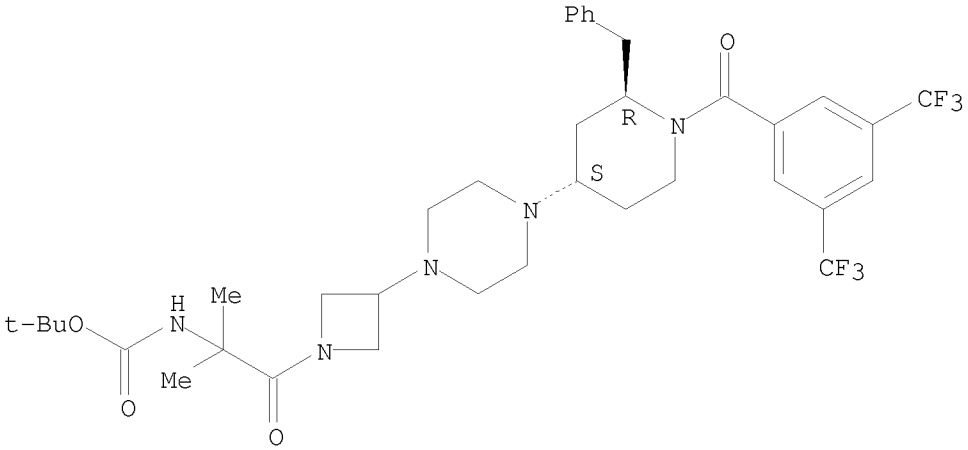
RN 718637-91-3 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(1-oxo-2-phenylpropyl)-3-azetidinyl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 718637-92-4 CAPLUS
CN Carbamic acid, [2-[3-[4-[(2R,4S)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-1-piperazinyl]-1-azetidinyl]-1,1-dimethyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.74	178.05

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.78	-0.78

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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L5 0 L3

=> file chemcats

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=> s l3
L6            0 L3

=> log h
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.93     179.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -0.78

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